PATENT COOPERATION TREAT

From the:
INTERN··TIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

TDC

Date of mailing *day/month/year*	5 JAN 2005
Applicant's or agent's file reference 12328250/TDO/FT	**IMPORTANT NOTIFICATION**

International Application No.	International Filing Date	Priority Date
PCT/AU2003/001154	5 September 2003	6 September 2002

Applicant

MEDVET SCIENCE PTY LTD et al

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translations to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide

Name and mailing address of the IPEA/AU	Authorized officer
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	JENNIFER FERNANCE Telephone No. (02) 6283 2269

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 12328250/TDO/FT	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International Application No. **PCT/AU2003/001154**	International Filing Date *(day/month/year)* 5 September 2003	Priority Date *(day/month/year)* 6 September 2002

International Patent Classification (IPC) or national classification and IPC

Int. Cl. [7] A61K 38/45, 31/4355, 31/407, A61P 03/04, 09/14, 27/00, 29/00, 35/04

Applicant

MEDVET SCIENCE PTY LTD et al

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheet(s).

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand 6 April 2004	Date of completion of the report 21 December 2004
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **JENNIFER FERNANCE** Telephone No. (02) 6283 2269

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/AU2003/001154

I. Basis of the report

1. With regard to the **elements** of the international application:*

[X] the international application as originally filed.

[ ] the description, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of

[ ] the claims, pages , as originally filed,
pages , as amended (together with any statement) under Article 19,
pages , filed with the demand,
pages , received on with the letter of

[ ] the drawings, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of

[ ] the sequence listing part of the description:
pages , as originally filed
pages , filed with the demand
pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. [ ] The amendments have resulted in the cancellation of:

[ ] the description, pages

[ ] the claims, Nos.

[ ] the drawings, sheets/fig.

5. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims -	**YES**
	Claims 1-48	**NO**
Inventive step (IS)	Claims -	**YES**
	Claims 1-48	**NO**
Industrial applicability (IA)	Claims 1-48	**YES**
	Claims -	**NO**

2. Citations and explanations (Rule 70.7)

The following documents identified in the International Search Report have been considered for the purposes of this report:

D1. The Merck Index (12th ed). Published by Merck & CO., INC. Entry 886: Aspirin.

D2. Frey et al., (2002). PKCζ regulates TNF-α-induced activation of NADPH oxidase in endothelial cells. Circulation Research 90:1012-1019.

D3. Rahman et al., (2000). Protein kinase C-ζ mediates TNF-α-induced ICAM-1 gene transcription in endothelial cells. American Journal of Physiology. Cell Physiology 279:C906-C914.

D4. Wellner et al., (1999). The proliferative effect of vascular endothelial growth factor requires protein kinase C-α and protein kinase C-ζ. Arteriosclerosis, Thrombosis and Vascular Biology 19(1):178-185.

D5. US 6410597 B1 (Bieberich et al.), June 25 2002.

D6. US 2002/0091082 A1 (Aiello), July 11 2002.

Claims 1-14 define a method of modulating endothelial cell activity through modulating the functional activity of protein kinase Cζ (PKCζ). Claims 15-26 define a method of regulating endothelial cell activity through modulating the functional activity of PKCζ. Claims 27-41 define a method of prophylaxis or treatment of a condition associated with altered endothelial cell activity, through modulating the functional activity of PKCζ. Claim 42 and appended claims 43-44 and 46 are considered to be of similar scope to claim 15, and claim 45 defines a method of regulating endothelial cell activity using PKCζ or a nucleic acid encoding PKCζ. Claim 48 claims any modulatory agent in pharmaceutical form.

Novelty (N) Claims 1-48

D1 deprives speculative claim 48 of novelty. Aspirin is perhaps the best known modulatory agent. It is often formulated as a pharmaceutical with pharmaceutically acceptable carriers.

D2 discloses that inhibition of PKCζ effectively modulates/regulates TNF-α induced endothelial cell function *in vitro*, and therefore deprives claims 1-41 of novelty. See the whole document, particularly the abstract, figures 4-7 and the last paragraph of the discussion.

D3 Discloses modulation of PKCζ using dominant negative mutants, antisense oligonucleotides and PKCζ in endothelial cellsError! Reference source not found. (see the whole document). Therefore claims 1-26 are considered to be deprived of novelty.

D4 disclose that PKCζ mediates vascular endothelial growth factor angiogenic effects in endothelial cells, using antisense oligonucleotides to PKCζ. Therefore claims 1-26 are considered to be deprived of novelty.

(continued in Supplemental page)

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claim 48 is not supported by the description due to the broad nature of claiming.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V

D5 deprives speculative claim 48 of novelty. It provides PKCζ modulators. D5 does not suggest modulation of endothelial cell activity.

D6 provides methods of treating disorders associated with/of the vascular endothelium by modulating PKCζ activity (see the whole document, particularly paragraphs 4, 6-10, 16, 26, 32-41, 46, 70, 63-156, and examples 8-11. Therefore claims 1-48 are considered to be deprived of novelty.

Inventive Step (IS) Claims 1-48

Claims 1-48 have already been found wanting of novelty, and are also considered to be deprived of an inventive step for the reasoning as above.

In addition:

D2 suggests that the method of treatment as claimed in claims 42 and 45 (see the last paragraph of the discussion), and therefore deprives said claims of an inventive step. Furthermore, the added features of appended claims 43-44 and 46 are not considered to import any patentability.

D3 teaches that PKCζ mediates TNF-α mediated inflammatory events in endothelial cells (see the whole document), and suggests that PKCζ is an important target in preventing the proinflammatory effects of TNF-α including adhesion molecule expression and subsequent neutrophil adhesion (see last paragraph of the discussion). Therefore claims 42 and 45 are considered to be deprived of an inventive step. Furthermore, the added features of appended claims 43-44 and 46 are not considered to import any patentability.

D4 does not suggest a method of treatment using PKCζ inhibitors/modulators.

D5 does not suggest modulation of endothelial cell activity.

Industrial Applicability (IA) Claims 1-48

Claims 1-48 appear industrially applicable. A method of modulating PKCζ mediated pathologies is provided.